IN THE CLAIMS:

Claim 1. (Currently Amended) ~~An algorithm~~ method for determining neuronal structure by analyzing a plurality of microscopy images of dendrites and spines in a computing device, said ~~algorithm~~ method comprising the steps of:

~~in a processing module,~~ processing the image~~s~~, by directing the computing device to automatically extract~~ing~~ representations of neuronal structures ~~there~~from the processed images, the extracting being performed based on geometrical features of the neuronal structures;

repeating said processing ~~module~~ steps for a plurality of microscopy images imaged over a sequence of time intervals; ~~and~~

tracing each extracted neuronal structure through a time-series of said images; and

~~in an analyzing module,~~ analyzing the extracted neuronal structures to determine at least one characteristic thereof.

Claim 2. (Currently Amended) The ~~algorithm~~ method according to Claim 1, wherein ~~the~~ an image is selected from the group consisting of static image and time-series images.

Claim 3. (Currently Amended) The ~~algorithm~~ method according to Claim 1, wherein the processing module performs ~~a~~ deconvolution and segmentation processes to extract the neuronal structures.

Claim 4. (Currently Amended) The ~~algorithm~~ method according to Claim 3, wherein the extracted neuronal structures include a plurality of dendrites which are identified via their respective backbones.

Claim 5. (Currently Amended) The ~~algorithm~~ method according to Claim 4, wherein the processing module detects from the plurality of dendrites a plurality of spines as geometric protrusions relative to the backbones.

Claim 6. (Currently Amended) The ~~algorithm~~ method according to Claim 5, wherein the processing module subjects each geometric protrusion to a protrusion criterion to

distinguish geometric protrusions associated with the plurality of spines from geometric protrusions not associated with the plurality of spines.

Claim 7. (Currently Amended) The ~~algorithm~~ method according to Claim 6, wherein the processing module correlates each detached spine of the plurality of spines to its respective dendrite of the plurality of dendrites.

Claim 8. (Currently Amended) The ~~algorithm~~ method according to Claim 5, wherein the analyzing module analyzes each of the plurality of spines to determine the at least one characteristic thereof.

Claim 9. (Currently Amended) The ~~algorithm~~ method according to Claim 8, wherein the at least one characteristic thereof is selected from the group consisting of spine length, spine density and spine volume.

Claim 10. (Currently Amended) The ~~algorithm~~ method according to Claim 9, wherein the spine length for a spine detached from its respective dendrite is determined by the distance from a recorded dendrite surface volume element corresponding to the respective dendrite to a furthest spine volume element corresponding to the detached spine.

Claim 11. (Currently Amended) The ~~algorithm~~ method according to Claim 9, wherein the spine length for a spine fully or partially attached to its respective dendrite is determined by the distance from the center of mass corresponding to base boundary points associated with the fully or partially attached spine to a furthest spine volume element corresponding to the fully or partially attached spine.

Claim 12. (Currently Amended) The ~~algorithm~~ method according to Claim 9, wherein the spine density is computed as the number of spines per unit length of dendritic backbone.

Claim 13. (Currently Amended) The ~~algorithm~~ method according to Claim 9, wherein the spine volume is computed by multiplying the ratio of maximum spine intensity to maximum dendrite intensity by focal volume.

Claim 14. (Currently Amended) The ~~algorithm~~ method according to Claim 5, wherein the analyzing module classifies each of the plurality of spines according to shape.

Claim 15. (Currently Amended) The ~~algorithm~~ method according to Claim 14, wherein each of the plurality of spines is classified in one of the following classifications: stubby, thin and mushroom.

Claim 16. (Currently Amended) The ~~algorithm~~ method according to Claim 14, wherein the analyzing module determines the shape of each of the plurality of spines based on spine length, spine head diameter and spine neck diameter.

Claim 17. (Currently Amended) The ~~algorithm~~ method according to Claim 16, wherein a spine is classified as a thin spine if the spine length is greater than the neck diameter; a spine is classified as a stubby spine if the neck diameter is approximately equal to the spine length; and a spine is classified as a mushroom spine if the spine length does not exceed neck diameter by more than a factor of 5 and the head diameter is greater than the neck diameter.

Claim 18. (Currently Amended) A method for determining the effect of a substance on ~~a~~ one or more neurons comprising the steps of:

subjecting the neurons to the substance;

imaging the neurons to generate at least one image including a statistically significant population of neuron structures;

~~subjecting the at least one image to an algorithm which contains~~

~~(i) a processing module for~~ processing the image and extracting neuronal structures therefrom based on geometrical features of the neuronal structures; ~~and~~

~~(ii) an analyzing module for~~ analyzing the extracted neuronal structures to determine at least one characteristic thereof; and

utilizing statistical inference tests to compare ~~comparing~~ the at least one characteristic from the population of neuron structures to a corresponding at least one characteristic from a population of corresponding structures of a control neuron, thereby determining the effect of a substance on a neuron.

Claim 19. (Original) A method for determining the effect of a substance on a neuron according to claim 18, wherein subjecting the neuron to the substance involves entry of the substance into the neuron.

Claim 20. (Original) A method for determining the effect of a substance on a neuron according to claim 19, wherein the entry is accomplished by a transfection technique selected from the groups consisting of diffusion, electroporation, viral transfer, lipid mediated transfer, calcium phosphate precipitation, direct injection and biollistic transfer.

Claim 21. (Original) A method for determining the effect of a substance on a neuron according to claim 18, wherein the image is generated by laser scanning microscopy.

Claim 22. (Original) A method for determining the effect of a substance on a neuron according to claim 21, wherein the laser scanning microscopy is selected from the group consisting of 2-photon exitation laser scanning microscopy and confocal laser scanning microscopy.

Claim 23. (Original) A method for determining the effect of a substance on a neuron according to claim 18, wherein the neuron is contained in a brain slice.

Claim 24. (Original) A method for determining the effect of a substance on a neuron according to claim 18, wherein the image is selected from the group consisting of static image and time-series images.

Claim 25. (Currently Amended) A method for determining the effect of a substance on a neuron according to Claim 18, wherein the processing module performs ~~a~~ deconvolution and segmentation processes to extract the neuronal structures.

Claim 26. (Original) A method for determining the effect of a substance on a neuron according to Claim 25, wherein the extracted neuronal structures include a plurality of dendrites which are identified via their respective backbones.

Claim 27. (Original) A method for determining the effect of a substance on a neuron according to Claim 26, wherein the processing module detects from the plurality of dendrites a plurality of spines as geometric protrusions relative to the backbones.

Claim 28. (Original) A method for determining the effect of a substance on a neuron according to Claim 27, wherein the processing module subjects each geometric protrusion to a protrusion criterion to distinguish geometric protrusions associated with the plurality of spines from geometric protrusions not associated with the plurality of spines.

Claim 29. (Original) A method for determining the effect of a substance on a neuron according to Claim 28, wherein the processing module correlates each detached spine of the plurality of spines to its respective dendrite of the plurality of dendrites.

Claim 30. (Original) A method for determining the effect of a substance on a neuron according to Claim 27, wherein the analyzing module analyzes each of the plurality of spines to determine the at least one characteristic thereof.

Claim 31. (Original) A method for determining the effect of a substance on a neuron according to Claim 30, wherein the at least one characteristic thereof is selected from the group consisting of spine length, spine density and spine volume.

Claim 32. (Original) A method for determining the effect of a substance on a neuron according to Claim 31, wherein the spine length for a spine detached from its respective dendrite is determined by the distance from a recorded dendrite surface volume element corresponding to the respective dendrite to a furthest spine volume element corresponding to the detached spine.

Claim 33. (Original) A method for determining the effect of a substance on a neuron according to Claim 31, wherein the spine length for a spine fully or partially attached to its respective dendrite is determined by the distance from the center of mass corresponding to base boundary points associated with the fully or partially attached spine to a furthest spine volume element corresponding to the fully or partially attached spine.

Claim 34. (Original) A method for determining the effect of a substance on a neuron according to Claim 31, wherein the spine density is computed as the number of spines per unit length of dendritic backbone.

Claim 35. (Original) A method for determining the effect of a substance on a neuron according to Claim 31, wherein the spine volume is computed by multiplying the ratio of maximum spine intensity to maximum dendrite intensity by focal volume.

Claim 36. (Original) A method for determining the effect of a substance on a neuron according to Claim 27, wherein the analyzing module classifies each of the plurality of spines according to shape.

Claim 37. (Original) A method for determining the effect of a substance on a neuron according to Claim 36, wherein each of the plurality of spines is classified in one of the following classifications: stubby, thin and mushroom.

Claim 38. (Original) A method for determining the effect of a substance on a neuron according to Claim 36, wherein the analyzing module determines the shape of each of the plurality of spines based on spine length, spine head diameter and spine neck diameter.

Claim 39. (Original) A method for determining the effect of a substance on a neuron according to Claim 38, wherein a spine is classified as a thin spine if the spine length is greater than the neck diameter; a spine is classified as a stubby spine if the neck diameter is approximately equal to the spine length; and a spine is classified as a mushroom spine if the spine length does not exceed neck diameter by more than a factor of 5 and the head diameter is greater than the neck diameter.

Claim 40. (Original) A method for determining the effect of a substance on a neuron according to Claim 18, wherein the substance is selected from the group consisting of nucleic acid, protein, peptide, carbohydrate, lipid, metal, radiation, temperature, pH, drug, toxin, dye, virus, vitamin and mineral.

Claim 41. (Original) A method for determining the effect of a substance on a neuron according to Claim 18, wherein subjecting the neuron to the substance includes exposure of the neuron to at least two dyes such that one dye illuminates the structure of a dendrite and a second dye illuminates distribution of a target molecule in the neuron.

Claim 42. (Original) A method for determining the effect of a substance on a neuron according to Claim 41, wherein the second dye is a fusion protein comprising a fluorescent protein linked to a target protein of interest.

Claim 43. (Currently Amended) A method for determining a structure by analyzing a microscopy image, said method comprising the steps of:

a) ~~procuring~~ an image of a plurality of structures at a point in time;

b) ~~de-~~deconvolving and ~~de-~~desegmenting said image to produce an improved image of said plurality of structures without noise and background interferences;

c) identifying each structure of said plurality of structures and drawing a line through a medial axis construction of said structure;

d) detecting a plurality of sub-structures protruding from each said identified structure, wherein said sub-structures are attached and non-attached to said structure;

e) filtering said sub-structures protrusions to eliminate spurious sub-structures and combining irregular sub-structures according to a predefined criteria; and

f) repeating steps (a) through (e) for a plurality of points in time and tracing each said identified structure through a time-series of said images, wherein a sequence of each of said plurality of structures is imaged over a sequence of time intervals, thereby determining a structure.

Claim 44. (Previously Added) The method of claim 43, wherein said structures are neuron structures.

Claim 45. (Previously Added) The method of claim 44, wherein said improved image is a dendritic phase of said plurality of neuron structures.

Claim 46. (Previously Added) The method of claim 45, wherein said medial axis construction is a backbone and said identified structures are dendrites.

Claim 47. (Previously Added) The method of claim 46,wherein, said plurality of sub-structures are spines detected as geometric protrusions relative to said backbone.

Claim 48. (Previously Added) The method of claim 43, further comprising a step of extracting morphological characterizations of said sequence of each of said plurality of structures.